Versar inc.

MEMORANDUM

TO: Srinivas Gowda

cc: 4600.013
Doreen Aviado

FROM: Mike Huang/Pat Wood

DATE: November 20, 2000

SUBJECT: Review of *Abiotic Degradation: Hydrolysis as Function of pH* in the Study Report S123396: Preliminary Chemical Characterization and Physical Chemical Data. Project 504624

This study report has been submitted to satisfy the requirements specified by the U.S. Environmental Protection Agency (i.e., the Agency) under Subdivision N (ENVIRONMENTAL FATE) of the Pesticide Assessment Guidelines. The Study Report provides data from the analyses on identity, physico-chemical properties, abiotic degradation (hydrolysis), and stability for the test substance. This review provides an assessment of the hydrolysis data only. The hydrolysis of N-n-Butyl-1,2-Benzisothiazolin-3-one in the aquatic solution has been reviewed for compliance with the EPA Environmental Fate Guidelines 160-4 and 161-1. The following information can be used to identify this study:

Title:	S123396: Preliminary Chemical Characterization and Physical Chemical Data. Project 504624
Action No.:	WO31
Author(s):	T.M. Williams
Date:	April 1996
MRID No.:	443649-02
Sponsor:	J.H. Moore SHE ZENECA Specialties Hexagon House Blackley Manchester M9 8ZS
Performing Laboratory/ Testing Facility:	ZENECA Specialties Analytical Sciences Group, Specialities Research Centre Hexagon House Blackley Manchester M9 8ZS
Study No.:	Project 504624
Primary Reviewer:	Mike Huang, Ph.D. Versar, Inc.
Approximate Technical Labor Hours:	30 hours
Chemical:	N-n-Butyl-1,2-Benzisothiazolin-3-one
DP Barcode:	D270035
EPA Receiving Date:	August 19, 1997

DATA EVALUATION RECORD

1.0 SUMMARY AND CONCLUSIONS

Hydrolysis of N-n-butyl-1,2-benzisothiazolin-3-one in aqueous solutions at pH 4, 7, and 9 was studied according to the method published by the Official Journal of the European Communities. The test substance was a blend of five individual samples manufactured at Huddersfield Works, ZENECA Fine Chemicals Manufacturing Organization. The sample contained 95.5 percent of N-n-butyl-1,2-benzisothiazolin-3-one and 4.3 percent of other organic impurities. The hydrolysis study was conducted at 50°C in pH buffer solutions containing 1 percent of methanol because of the limited water solubility of n-butyl-1,2-benzisothiazolin-3-one. The hydrolysis was monitored by taking small aliquots of solutions at time intervals of 0, 0.875, 1.875, 4.875, and 6 days and N-n-butyl-1,2-benzisothiazolin-3-one was analyzed using HPLC.

The study indicated that no significant hydrolysis of N-n-butyl-1,2-benzisothiazolin-3-one was detected at results pH 4 and pH 7. Approximately 4 to 5 percent hydrolysis was detected at pH 9. In the study, half-lives were not calculated because the percent of hydrolysis was less than 10 percent. According to the report, a loss of less than 10 percent in 5 days is equivalent to a half life of greater than 1 year at 25°C. However, no calculation procedure for such a conversion was provided. (Note that the study was carried out at 50°C, while the half life was estimated at 25°C.)

The study was generally in compliance with the EPA Environmental Fate Guidelines 161-1 – Hydrolysis Studies and 160-4 – General Test Standards. Major deviations from EPA Guidelines 160-4 and 161-1 were identified as follows:

- *The temperature of hydrolysis reaction should be maintained at 25 ± 1 °C.* The hydrolysis study was conducted at 50°C in this study.
- *Hydrolysis experiments should be carried out in solutions buffered at pHs 5, 7, and 9.* The hydrolysis experiments were conducted at pHs 4 , 5, and 9. An explanation was not given for using pH 4 rather than pH 5 to test the hydrolysis of the test substance.
- *The water used for this study should be free of all live bacteria, and the glassware should be sterilized to minimize the possibility of microbial degradation of the test substance.* Information was not provided in the study to indicate that such a requirement was met, although such a procedure might have been included in the method used in the study.

- *A maximum of 30 days of monitoring is permitted.* It could not be determined from the Study Report if sample aliquots had been taken at sufficient sampling time intervals to define decline of the test substance. In this study, hydrolysis was monitored for a total of 6 days.

- *Laboratory hydrolysis study should be conducted in darkness.* It could not be determined from the Study Report if this condition was met.

2.0 METHODOLOGY

The hydrolysis study was conducted according to the following method:

- Methods for the Determination of Physico-Chemical Properties. Official Journal of the European Communities L383A, Vol. 35, 29th December 1992.

The Study Report provided a very brief description of the method. Hydrolysis of the test substance was studied at pHs 4, 7, and 9. The solutions of test substance were prepared in pH buffered solutions and stored in an oven at 50°C. As the test substance has no appreciable aqueous solubility (<0.0005 g/L), methanol was added so that the solutions contained 1 percent (v/v) of methanol. At different time intervals, small aliquots of samples were taken from the solutions and analyzed for N-n-butyl-1,2-benzisothiazolin-3-one using high performance liquid chromatography (HPLC). Hydrolysis was monitored for a total of 6 days.

2.1 Apparatus

The HPLC instrument model HP1090M was used to analyze the test substance. However, detailed information on instruments and devices used in the study was not provided.

2.2 Test Substances and Reagents

Five samples from individual lots of test substances and a blend of all the five samples were used in the overall study. However, only the blend sample was used in the hydrolysis study. The test substance was manufactured at Huddersfield Works, ZENECA Fine Chemicals Manufacturing Organization. The blend sample was found to contain 95.5 percent of N-n-butyl-1,2-benzisothiazolin-3-one. The composition of the blend sample is provided in Table 1.

The pH buffer solutions were prepared as follows:

- pH 4 Buffer Solution – 164 ml of 0.2 M glacial acetic acid with 36 ml of 0.2 M sodium acetate was diluted to 1 liter with distilled water;
- pH 7 Buffer Solution – 296 ml of 0.1 M sodium hydroxide with 500 ml of 0.1 M mono-potassium phosphate was diluted to 1 liter with distilled water;
- pH 9 Buffer Solution – 213 ml of 0.1 M sodium hydroxide with 500 ml of 0.1 M boric acid was diluted to 1 liter with distilled water.

Table 1. Composition of the Test Substance (Blend Sample)

Components	Contents
Water Content	< 0.1 percent (w/w)
Sulfated Ash	<0.1 percent (w/w)
The main component – N-n-butyl-1,2-benzisothiazolin-3-one	95.5 percent (w/w)
The major impurity – N-ButylBisamide	4.8 percent (w/w)
Other organic impurities	1.3 percent (w/w)
Organic Purity	99.8 percent (w/w)

2.3 Calibration, Standardization, and Operating Conditions of HPLC

HPLC was used to determine the test substance in this study. However, the procedures and standards used for calibration were not provided in the Study Report. The operating conditions of HPLC were provided and re-summarized in Table 2.

Table 2. HPLC Operating Conditions

Instrument:	HP1090M		
Column:	25cm × 0.32 cm Spherisorb S5 ODS-1		
Column Oven:	40 °C		
Mobile Phase:	Eluent A: Distilled Water: Acetonitrile: Methanol: Glacial Acetic Acid = 60:25:20:2.5 Eluent B: Acetonitrile: Methanol: Glacial Acetic Acid = 54:45:2.5		
Gradient Profile:	**Time (minutes)**	**% A**	**%B**
	0.00	100	0
	12.00	25	75
	15.00	25	75
	16.00	100	0
	21.00	100	0
Detective Wavelength:	254 nm		
Injection Volume:	10 µl		
Flow rate	0.75 ml/minute		

2.4 Procedure

The hydrolysis study was conducted according to the following procedures:

1. Two stock solutions (25 ml each) of test substance were prepared using methanol;
2. Duplicate test solutions (TEST A and TEST B) were prepared by dilution of 1.0 ml of each stock solution to 100.0 ml with the appropriate buffer solutions;
3. Test solutions were placed in an oven at 50°C after taking small aliquots for initial analysis;
4. Small aliquots of solutions were taken at intervals of 0.875, 1.875, 4.875, and 6 days;
5. Samples were anayzed for the main component of the test substance – N-n-Butyl-1,2-Benzisothiazolin-3-one, using HPLC.

3.0 DATA SUMMARY

The hydrolysis study results are provided in the Study Report and re-summarized in Table 3 of this review report. No significant hydrolysis of the test substance was detected at pH 4 and 7 after maintaining test solutions in an oven at 50°C for 6 days. However, 4 to 5 percent of loss of the test substance due to hydrolysis was observed at pH 9. Since the percent loss of the test substance was less than 10 percent, the half-life of hydrolysis was not calculated. According to the Study Report, the less than 10 percent loss of the test substance in 5 days was estimated to be equivalent to a half-life of more than one year at a more representative field temperature of 25°C. However, the study did not provide the procedure for converting ~10 percent loss of the test chemical at 50°C to a half-life of more than 1 year at 25°C.

Table 3. Data Summary on Hydrolysis of N-n-Butyl-1,2-Benzisothiazolin-3-one

Time (days)	TEST 1		TEST 2	
	Concentrations (g/L)	Percent of Loss (%)	Concentrations (g/L)	Percent of Loss (%)
pH 4 at 50°C				
0	0.0288	–[a]	0.0281	–
0.875	0.0293	–	0.0282	–
1.875	0.0292	–	0.0284	–
4.875	0.0299	–	0.0289	–
6	0.0297	–	0.0288	–
pH 7 at 50°C				
0	0.0291	–	0.0282	–
0.875	0.0293	–	0.0283	–
1.875	0.0292	–	0.0284	–
4.875	0.0296	–	0.0290	–
6	0.0294	–	0.0286	–
pH 9 at 50°C				
0	0.0295	–	0.0287	–
0.875	0.0290	2	0.0282	2 (Test 1 & 2)
1.875	0.0288	2	0.0281	2 (Test 1 & 2)
4.875	0.0283	4	0.0282	4 (Test 1) 2 (Test 2)
6	0.0281	5	0.0277	5 (Test 1) 4 (Test 2)

a – No loss was detected in solutions at pH 4 and pH 7.

4.0 COMMENTS

EPA Environmental Fate Guidelines 161-1(i.e., Hydrolysis Study) and 160-4 (i.e., General Test Guidelines) were generally followed in this hydrolysis study. The main discrepancies are identified as follows:

- *The temperature of hydrolysis reaction should be maintained at 25 ± 1 ℃.* The hydrolysis study was conducted at 50°C in this study.

- *Hydrolysis experiments should be carried out in solutions buffered at pHs 5, 7, and 9.* The hydrolysis experiments were conducted at pHs 4 , 5, and 9. An explanation was not given for using pH 4 rather than pH 5 to test the hydrolysis of the test substance.

- *The water used for this study should be free of all live bacteria, and the glassware should be sterilized to minimize the possibility of microbial degradation of the test substance.* Information was not provided in the study to indicate that such a requirement was met, although such a procedure might have been included in the method used in the study.

- *A maximum of 30 days of monitoring is permitted.* It could not be determined from the Study Report if sample aliquots had been taken at sufficient sampling time intervals to define decline of the test substance. In this study, hydrolysis was monitored for a total of 6 days.

- *Laboratory hydrolysis study should be conducted in darkness.* It could not be determined from the Study Report if this condition was met.

ATTACHMENT

Test Substance Identity

1. IDENTITY OF SUBSTANCE

1.1 Name

1.1.1 IUPAC Name

2-Butyl-benzo[d]isothiazol-3-one

1.1.2 Common Names

N-n-butyl-1,2-benzisothiazolin-3-one

N-Butyl BIT

1.1.3 CAS Registry Number

4299-07-4

1.1.4 Code Numbers

S123386.

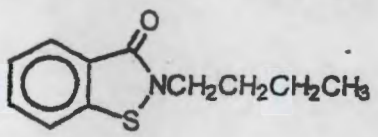
1.2 Empirical and Structural Formula

1.2.1 Empirical

$C_{11}H_{13}NOS$

1.2.2 Structural

The main component of the test substance has the identity given below:



1.2.3 Molecular Weight

207.30